

THE WORLD OF CHEMISTRY

Program #24

THE GENETIC CODE

Producer Stephen Redhead

Air Script: October 31, 1988

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Annenberg/CPB Project Logo and Music

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MONTAGE: Child in hospital,
computer models, family
walking

NARRATOR (MUSIC and NAT
SOUND under):

This young girl suffers from a hereditary disease. She inherited it from her parents and will carry it for the rest of her life. There is no cure for this disease, but its symptoms can be successfully treated. The disease is the result of a small chemical change in one of the vital proteins in her body. How did this change come about? How does the body manufacture all the proteins it requires to sustain life, and why do mistakes occur? The answer lies in the chemical instructions at the heart of all living things, the genetic code.

SUPER: THE GENETIC
CODE

THE WORLD OF CHEMISTRY OPEN: Montage, Music, Logo

RH in office with chemical models

ROALD HOFFMANN (SYNC):
Proteins can be structural elements like hair, or wool, or muscle, or they can be the little chemists in our bodies in enzymes. But they can also do more. In fact, the one protein about which we know much more than any other one is not a structural protein, nor an enzyme, but it's a transport protein. It takes a molecule from one part of the body to another one, but not just any molecule. This protein, hemoglobin, takes the life-giver oxygen from our lungs to every cell in our body. Hemoglobin is a remarkable molecule. It's made up of four subunits, each capable of binding oxygen, each a chain of amino acids, and in each subunit there is a molecule called a heme, in which, in the middle of all this organic complexity, there is sitting at the center an iron atom which binds the oxygen. Now you can see why iron is needed for good blood. In this program we're going to learn more about hemoglobin and about a molecular disease called sickle cell anemia.

MONTAGE: Sunrise, nature shots, children playing, baby, athletes, computer models, hospital, people eating, microscopic cells

NARRATOR (MUSIC and NAT SOUND under):

Life is a chemical condition. Living things are composed of lifeless molecules. Isolated and examined individually, these molecules conform to all the physical and chemical laws that describe the behavior of inanimate matter. Bound up together in exquisite complexity, these same molecules are responsible for life itself. How do these collections of molecules interact to maintain the living state? Proteins, with their many different biological functions, are largely responsible for this coordinated effort. Proteins do almost everything in the body. They form important structural tissues, and muscles. As enzymes, they catalyze and regulate chemical reactions, and as hormones, coordinate many bodily functions. All of this requires energy. Like other animals, we obtain our energy from food. Inside the cells in our bodies, tiny chemical factories use the oxygen we breathe to release energy from food molecules. How does this vital oxygen get from the lungs to the cells? It is carried in the blood by a transport protein, hemoglobin. (cont.)

NARRATOR cont:

The oxygen binds to the iron in the hemoglobin, contained within the disc-like red blood cells. Hemoglobin is the red pigment that gives blood its characteristic color. Dr. Jacqueline Barton of Columbia University.

INTERVIEW: Dr. Jacqueline Barton, Columbia University

SUPER: Dr. Jacqueline Barton

DR. JACQUELINE BARTON (SYNC):
Hemoglobin is, is a really remarkable protein, and it's actually quite a complicated protein, but one that chemists have been studying for, for a good number of years by this stage. Now, hemoglobin is, is in some respects complicated because it is really four polypeptides, it has four different units within it, and those polypeptides are of two types, all right. There's actually an alpha type and then there's a beta type.

MONTAGE: Microscopic cells, models, computer models

NARRATOR (MUSIC under):
Each hemoglobin molecule contains two alpha chains and two beta chains closely bound together. Proteins, like hemoglobin, with two or more polypeptide chains, therefore have four levels of structural complexity. (cont.)

NARRATOR cont:

A primary structure, referring to the amino acid sequence in each chain; a secondary structure, which refers to the organization of sections of the chains into alpha helices and beta sheets; a tertiary structure, in which each chain folds up into a compact globular unit; and finally, a quaternary structure, which refers to the way the individual polypeptide chains pack together.

Computer models

NARRATOR (MUSIC under):

Here is hemoglobin with its four polypeptide chains, each bonded to a heme molecule, shown in red. At the center of each heme lies a single iron atom, to which an oxygen molecule bonds. So each hemoglobin molecule can bind a total of four molecules of oxygen, and it does this in a most elegant and efficient way. The first oxygen to bind to a heme group causes a slight change in the packing arrangement of the polypeptide chains. This new arrangement increases the affinity of the second heme group for oxygen. A second oxygen binds, causing a further structural change, which increases the oxygen affinity for the third heme group, and so on, until four oxygen molecules are bound.

INTERVIEW: Dr. Jacqueline
Barton cont.

DR. JACQUELINE BARTON (SYNC):
Hemoglobin is really an excellent
example of the relationship between
structure and function, because what, as,
as we understand those various
structural changes that occur in binding
oxygen to one site and causing the
changes that have got to occur in the
structure, then we can understand the
functional aspects of that, how that
protein changes to let you know that the
other domain, the other domain is now
gonna be cooperating in binding the
next, the next molecule of oxygen.

Computer models

NARRATOR:
At the heart of this complex interplay
between protein structure and function is
the primary structure, for it is the amino
acid sequence that determines the higher
levels of protein structure and thus,
function. This has profound
consequences. Change a single amino
acid and the resulting alteration in
structure may severely affect the
protein's biological function.

African life, children
playing

NARRATOR (NAT SOUND under):
This is dramatically demonstrated in the hereditary disease, sickle cell anemia, a disorder involving hemoglobin. Sickle cell anemia is very common in West Africa, where locally as many as 40 percent of the children are born with it. Madeline Taylor and her husband both have the disease. They grew up in Africa and now live in the United States, where an estimated one in every 625 American blacks suffer from this hereditary disorder.

Taylor children playing

MADELINE TAYLOR (VO/SYNC):
In Africa, we don't talk much about sickle cell. When you have it, it's a hush-hush, people don't talk about it, and people don't want you to know about it, because it's considered a bad disease.

INTERVIEW: Madeline
Taylor

SUPER: Madeline Taylor

When I came to the United States, I still wasn't able to talk about it, until my first child was born, Nadeline, and she came down with the disease. She had a crisis. They call it the hand and foot syndrome in babies. (cont.)

MADELINE TAYLOR cont:

She was only three months old at that time. So I took her to the Emergency Room at Holy Cross Hospital, then they found out that she had the disease and they referred us to Children's Hospital, and were tested all over myself, my husband, and the baby. Children's Hospital, they did their own testing.

Taylor children playing

NARRATOR (NAT SOUND under):

The disease has brought with it many complications for Nadeline. She has repeated bouts of infection, including pneumonia and meningitis. And at age 7, Nadeline had a stroke.

INTERVIEW: Madeline
Taylor cont.

MADELINE TAYLOR (SYNC):

I have worked in nursing homes. Okay. I've seen older people with stroke. I've taken care with people that have stroke. But I never knew, in all my years of being a little bit of nothing that the child can come down with a stroke. So it was very frightening for me.

Taylors in hospital
examining room

NARRATOR (NAT SOUND under):
But what causes the disease? The answer
is a change in the normal function of
hemoglobin. In people with sickle cell
anemia, the hemoglobin molecules have
a tendency to stick together. Gordon
Bray is Nadeline's pediatrician, and the
director of the sickle cell program at the
National Children's Hospital in
Washington, D.C.

INTERVIEW: Dr. Gordon
Bray, Director of the sickle
cell program, National Children's
Hospital, Washington, D.C.

SUPER: Dr. Gordon Bray

DR.GORDON BRAY (SYNC):
Hemoglobin molecules in red blood cells
exist in solution. They essentially are
free-floating. And when the red blood
cell is called upon to change shape or to
become deformed, hemoglobin
molecules tend not to interfere with that
process. Sickle hemoglobin has an
unusual propensity to self-assemble with
one another. In other words, the
molecules form aggregates.

Red blood cells, sickle cells,
computer models

NARRATOR (MUSIC under):

Here are some normal red blood cells containing hemoglobin in solution, and here are some sickle cells, in which the sticky hemoglobin molecules have crystallized and deformed the cells. These deformed cells are rigid, and so can block small blood vessels. They contain useless hemoglobin incapable of binding oxygen, and are responsible for the many symptoms of the disease. How does sickle hemoglobin differ from normal hemoglobin at the molecular level? Remarkably, these molecules only differ by a single amino acid. In normal hemoglobin, the sixth amino acid in each beta chain is negatively charged glutamate. In sickle hemoglobin, this has been replaced by the nonpolar amino acid, valine. This single change may seem insignificant, but it produces a crucial alteration in tertiary structure, which causes the sickling.

Taylor children playing

NARRATOR (NAT SOUND under):

As yet there is no cure for sickle cell anemia, but the symptoms are treatable. With modern drugs, and with blood transfusions to replace the sickle cells her body manufactures with normal red blood cells, Nadeline enjoys a relatively normal life.

RH in office

ROALD HOFFMANN (SYNC):

We've seen a disease, sickle cell anemia, traced to just a single amino acid mistake. It's genetically transmitted. What does that mean? Well, as a child is conceived, a sperm and egg cell from the parents unite, then multiply and differentiate, to give eventually the beautiful complexity of a newborn child. What the parents' give to the child is not a lot of protein or blood, it's genetic material. In the genes there is information to create all the protein that the child requires. But what are genes? Well, they're molecules, and, in particular, they're biopolymers. The genetic information, the coded library of life, is DNA, the biopolymer which we call deoxyribonucleic acid.

MONTAGE: Outdoor activities, computer models

NARRATOR (MUSIC and NAT SOUND under):

The intimate relationship between the primary structure of a protein and its biological function raises a more fundamental question. How does the body manufacture the many thousands of proteins it requires, and with such accuracy? One slip in the amino acid sequence can have profound consequences. (cont.)

NARRATOR cont:

How does sickle hemoglobin arise? The answer lies in nature's most remarkable molecule, DNA. All living things are composed of cells, and it is here that the DNA resides. Shaped like a spiral staircase, this beautiful molecule contains the chemical blueprint for making proteins. And proteins make living organisms.

INTERVIEW: Dr. Jacqueline Barton cont.

DR. JACQUELINE BARTON (SYNC):
Proteins are the chemists in the cell. DNA is actually the library of the cell. And DNA contains all the information that you need within the cell. Now, many of us know about DNA being important for heredity, and that code, based on your mother and your father's, was contained in each of your cells. But what's really important about DNA is that DNA actually codes for all the, all the proteins that are made within the cell, and that's really where we care and access the information that's on DNA all the time.

Computer models,
graphics: DNA
structure

NARRATOR:

So DNA contains the information for making proteins. But how does it do this? To understand its function, we must begin with its structure. DNA is nature's largest biopolymer, and it is made of nucleotides. Each nucleotide consists of a sugar, deoxyribose bonded to a phosphate group, and one of four nitrogen bases, either adenine, A, cytosine, C, guanine, G, or thymine, T. The nucleotides are hooked together through the phosphate groups, forming a long strand with a repeating sugar phosphate backbone and a sequence of nitrogen base side groups. Two strands of DNA are held together by hydrogen bonds that form between the A and T bases, and the C and G bases. The two strands then wind into a double helix. The sequence of bases is the chemical code for making specific polypeptides. But the relationship between the bases and the amino acids is not one-to-one, for there are only four bases, A, C, G, and T, and 20 amino acids. Instead, the code is based on a sequence of three bases. Each base triplet, GTC for instance, codes for one amino acid. A strand of DNA containing enough triplets to code for an entire polypeptide chain is called a gene.

Cells under microscope,
Encyclopaedia Britannica

NARRATOR (MUSIC under):

The amount of information contained within the DNA in one microscopic human cell is staggering, enough to fill the Encyclopaedia Britannica, all 30 volumes of it, four times over. The genetic code must then be transcribed onto a messenger molecule and taken from the nucleus of the cell, where the DNA resides, to the site of protein manufacture in the cytoplasm. The messenger, also a nucleotide polymer, is called messenger RNA.

GRAPHIC: The action
of messenger RNA

NARRATOR:

Synthesis of the messenger RNA begins when an enzyme, RNA polymerase, attaches to the DNA helix. The two strands separate and open. RNA nucleotides, which contain the sugar, ribose, with an additional OH group, hydrogen bond with a DNA strand, and covalently bond to each other, forming a single RNA strand. This process transcribes the chemical code from the DNA to the messenger RNA. RNA also differs from DNA in that the base, uracil, U, takes the place of thymine and pairs with adenine. (cont.)

NARRATOR cont:

The growing RNA strand carrying the chemical code for a specific protein, detaches from the DNA and leaves the nucleus for the site of protein synthesis.

Microscopic cells

NARRATOR (MUSIC under):

Protein synthesis is the most complex of all biochemical systems and requires the coordinated effort of many enzymes and other macromolecules. The polypeptide is assembled from the messenger RNA at a structure called a ribosome. The amino acids are carried by another type of RNA molecule, transfer RNA.

GRAPHIC: Transfer RNA
and the synthesis of proteins

NARRATOR:

The messenger RNA, shown here simplified, becomes attached to the ribosome, which contains all the enzymes and other initiating factors needed for polypeptide synthesis. Then a small transfer RNA molecule arrives, carrying the initiating amino acid. It has a base triplet that can only hydrogen bond to the messenger RNA triplet that codes for the amino acid it carries. Another transfer RNA, carrying a second amino acid, arrives and bonds to the next triplet. Again, the transfer RNA only bonds to the triplet that codes for the amino acid it is carrying. (cont.)

NARRATOR cont:

A peptide bond forms between the two amino acids. The first transfer RNA detaches and leaves as the ribosome moves to the next triplet in line. A third transfer RNA arrives and attaches to its triplet. The new amino acid now forms a peptide bond with the other two. The second transfer RNA leaves as the ribosome moves again. This process repeats itself over and over as the ribosome moves along the messenger RNA strand, translating the genetic code of base triplets into an amino acid sequence. Many ribosomes may attach to a single messenger RNA strand, resulting in the multiple copies of the same protein like hemoglobin that the body requires.

INTERVIEW: Dr. Jacqueline Barton cont.

DR. JACQUELINE BARTON (SYNC):
So really that amino acid sequence, that primary sequence of amino acids that's on that polypeptide was encoded in the DNA structure, because the DNA structure was responsible for the RNA, which was responsible for the protein. So the DNA contains all the information that's on that protein.

MONTAGE: Chemists at work in labs, computer models, city scenes, Taylor family, children with genetic diseases, plant research

NARRATOR (MUSIC and NAT SOUND under):

The biological function of all proteins, including hemoglobin, ultimately depends on the sequence of the bases in the gene. A change in the code, however slight, can have drastic consequences. At the heart of all the complications of sickle cell anemia lies a single base alteration.

EQUATIONS

The DNA base triplet, CTC, which codes for glutamate in normal hemoglobin, has been changed to CAC, which codes for valine. This change in the genetic code is passed on from generation to generation. That is why sickle cell anemia is called a hereditary disease. Sickle cell anemia is just one of almost 4,000 genetic diseases caused by a change in a single gene. Hemophilia, cystic fibrosis, and Tay-Sachs disease are other familiar examples, though none is as common as sickle cell. As yet, there is no cure for any genetic disease, for we have no way of correcting the defective gene, though some, like sickle cell, can be successfully treated. But the future holds great promise, thanks to a new technique called recombinant DNA technology. (cont.)

NARRATOR cont:

Scientists have discovered a special group of enzymes, restriction enzymes, which recognize specific base sequences in DNA and cut the strands at that point. This has made it possible to remove a gene from one DNA molecule and insert it into another. The genetic code can now be edited. This technology has already made important contributions to medical science. Genes coding for human insulin have been inserted into the DNA of bacteria, which are then grown in huge fermenting tanks. Here billions of bacteria act like human insulin factories, producing a virtually limitless supply of this important hormone. More and more diabetics are now injecting themselves with this human insulin rather than the animal insulin alternative, which can produce undesirable side effects. There are many who view recombinant DNA technology as the beginning of a new age in science. Laboratories throughout the world are already genetically modifying crop species, introducing genes that code for proteins that improve growth and protect the plant against insect pests. And scientists are hopeful that children with life-threatening genetic diseases may some day be cured by introducing normal copies of the defective gene into their cells. (cont.)

NARRATOR cont:

But recombinant DNA technology has even more to offer. It is allowing scientists to unravel chemistry's most remarkable secret, the molecular basis of life.

INTERVIEW: Dr. Jacqueline Barton cont.

DR. JACQUELINE BARTON (SYNC):
In some respects, you don't have to think about recombinant DNA technology as Woody Allen's world in "Sleeper," with oversized bananas and tomatos. That's not what recombinant DNA technology is all about. What it is all about is our learning how to manipulate and change macromolecular structure and, in so doing, learn an awful lot more about that macromolecular structure and the chemistry that nature's been doing all the time.

RH in library

ROALD HOFFMANN (SYNC):
In the coded library of the nucleus, the books of the human gene, resides tremendous potential: to reproduce, to make thousands of molecules, large and small, to respond in the infinite ways that the body has, to intruders, and to grow, using minimal input of chemicals and energy, a mind and a brain that is capable of writing millions of books, and paintings, and poems, and even of doing chemistry. (cont.)

ROALD HOFFMANN cont:

And, in this century, this tiny storehouse of information, expressing itself through many individuals, has followed the old injunction, "Know thyself," and so we have learned something about the way that we work. We listen to a song by the Beatles, we look at an Arizona sunset. Is it possible to know the sequence of firing of neurons and the biochemical actions in those neurons, and the chemistry and physics behind those actions? Is it possible to know scientifically a sunset, or a song, or our response to them? I think so. Does that scientific knowledge detract from our emotional response to the music? Not at all. These are different ways of understanding, different means of knowing, the chemistry is beautiful and so is the soul that responds to the music. In fact, it could be said that knowing about something scientifically enhances the emotional response.

Credits, Closing Montage, Closing Music

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